Table 1. MCII and PASS of pain and function instruments in hand OA patients in two settings.

Instrument	MCII (95% CI) in RCT†			PASS (95% CI)	
	Absolute units	Percentage	[n]	RCT (n=68)	Cohort (n=126)
MHQ					
Overall function, 0-100*	3.4 (-2.7;9.5)	3.6 (-9.1;16.3)	[23]	55.6 (52.6;58.5)	48.1 (45.7;50.4)
ADL, 0-100*	1.6 (-4.4;7.6)	2.8 (-9.6;15.3)	[23]	71.7 (68.2;75.1)	62.9 (59.8;66.0)
Pain, 0-100	-12.2 (-17.2;-7.1)	-23.1 (-35.4;-10.8)	[16]	47.0 (40.5;53.5)	55.7 (52.0;59.5)
AUSCAN					
Function, 0-36	-3.3 (-5.7;-0.9)	-9.8 (-23.9;4.2)	[23]	17.1 (15.3;19.0)	20.9 (19.4;22.3)
Pain, 0-20	-1.1 (-2.6;0.4)	-1.8 (-18.5;14.9)	[27]	9.0 (8.2;9.9)	11.1 (10.3;11.8)
FIHOA, 0-30	0.1 (-1.6;1.7)	22.7 (-0.7;46.0)	[23]	12.4 (11.1;13.7)	13.9 (12.8;15.0)
VAS pain, 0-100	-11.5 (-18.2;-4.7)	-24.4 (-36.1;-12.8)	[27]	47.7 (42.2;53.3)	48.8 (44.6;53.0)

Direction of effect of all instruments is higher is worse, except those with *.†For all MCII direction of effect was unified, so positive values indicate worse symptoms and negative values values indicate improved symptoms.

Conclusion: The only function instrument with an acceptable threshold for MCII was AUSCAN function, while for pain MHQ and VAS performed better than AUSCAN. PASS values show a relatively high level of tolerance of 50% of the maximum of the scale.

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POS0183 SIGLEC1 AS A TYPE I INTERFERON BIOMARKER IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Idiopathic inflammatory myopathies (IIM) are autoimmune diseases that mainly affect skeletal muscle, lung, skin and joints. IIM can be separated into dermatomyositis (DM), inclusion body myositis (IBM), antisynthetase syndrome (AS) and immune-mediated necrotizing myopathy (IMNM). Type I interferons (IFN) are known to play a crucial role in the etiopathogenesis of some of these entities such as DM.[1] Sialic acid binding Ig-like lectin 1 (SIGLEC1, CD169) is part of the type I IFN signature found in SLE and DM and is expressed on the cell surface of monocytes. Thus, analysis of SIGLEC1 expression by flow cytometry enables a straightforward assessment of the type I IFN signature. Its utility has been shown for juvenile and adult SLE and other rheumatic diseases but not in IIM.[2,3] The assessment of the type I IFN system in clinical practice is an unmet need and, in this context, SIGLEC1 might be useful.

Objectives: To assess SIGLEC1 expression on monocytes by flow cytometry as a type I IFN biomarker in IIM

Methods: Pediatric and adult patients with a clinical diagnosis of DM, AS, IMNM and IBM and at least one measurement of SIGLEC1 who have been treated at the Department of Rheumatology, Charité - Universitätsmedizin Berlin between 2015 and 2020 were included in this retrospective study. Control groups of healthy individuals (n=19) and SLE patients (n=30) were included. Disease activity was assessed by Physician Global Assessment (PGA) and Childhood Myositis Assessment Scale (CMAS). SIGLEC1 expression on monocytes was analyzed by flow cytometry. Cross-sectional analyses (n=74) were performed using Mann Whitney-U test (MWU) and two-level mixed-effects linear regression model was used for longitudinal analyses (n=26, 110 visits). This study was approved by the local ethics committee of the Charité - Universitätsmedizin Berlin.

Results: 74 patients (adult/juvenile DM: n=21/n=17; AS: n=19; IMNM: n=8; IBM: n=9) were included. In cross-sectional analysis, SIGLEC1 expression was significantly upregulated in adult and juvenile DM patients with moderate to severe disease activity (PGA≥5) compared with adult/juvenile DM patients with no to moderate disease activity (PGA<5) (both p<0.001). In longitudinal analyses, SIGLEC1 correlated with disease activity in juvenile DM (SIGLEC1 vs. CMAS: betaST=-0.65; p<0.001) and adult DM (SIGLEC1 vs. PGA: betaST=0.52; p<0.001), better than Creatine Kinase (CK) (juvenile DM, CK vs. CMAS: betaST=-0.50; p<0.001; adult DM, CK vs. PGA: betaST=0.17; p=0.149). In AS 42.1% of the patients showed elevated SIGLEC1 expression, while it was not upregulated in IMNM and only in two patients with IBM, who were concurrently positive for autoantibodies that affect the type I IFN system (see Figure 1).

Conclusion: SIGLEC1 is a useful biomarker to identify an activated type I IFN system in IIM. Flow cytometry is used widely in laboratory medicine, which could facilitate the implementation of SIGLEC1 into clinical routine.

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Figure 1. SIGLEC1 expression on monocytes in IIM subgroups and control groups; in IIM subgroups, patients with low disease activity (PGA<5) are marked in blue, patients with high disease activity (PGA≥5) are marked in red; mAb/cell, monoclonal antibodies bound per cell

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POS0184 URINE-GALECTINE 3 BINDING PROTEIN (U-GAL3BP) IS A SENSITIVE MARKER OF KIDNEY INFLAMMATION AND RESPONSE TO TREATMENT IN LUPUS

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Background: Lupus nephritis (LN) represents a serious manifestation of systemic lupus erythematosus (SLE) which requires timely diagnosis, treatment and monitoring. Kidney biopsy is the gold standard of diagnosis and is instrumental to treatment decisions, however it is not generally performed for monitoring and evaluation of response to treatment. To such purposes, accessible biomarkers, for instance urinary, might be highly advantageous.

Objectives: To evaluate urine-Galectin 3 binding protein (uGAL3BP) as a novel biomarker in biopsy-proven active lupus nephritis (A-LN) in comparison to active non-renal SLE (ANR-SLE), inactive SLE (I-SLE), and in population-based controls (HC). Furthermore, we compared uGAL3BP with known markers of renal pathology including neutrophil gelatinase-associated lipocalin (NGAL), osteopontin (OPN), kidney injury molecule 1 (KIM-1), and galectin 3 (GAL3).

Methods: Urine samples from A-LN (n=86), ANR-SLE (n=63), I-SLE (n=73) and HC (n=48) were included. uGAL3BP was measured using a commercial ELISA kit and values, adjusted for u-creatinine levels, were expressed as ng/mmol. Other markers analyzed according to clinical routine at the Department of Clinical Chemistry at Uppsala University Hospital were also adjusted for u-creatinine levels. Renal biopsies were graded according to the ISN/RPS classification(1) and evaluated for activity and chronicity index. Ten A-LN patients were evaluated before and after induction treatment.

Results: In the A-LN group, median (IQR) levels of u-GAL3BP were 15.8 (6.8-24.6) ng/mmol, while in ANR-SLE, I-SLE, HC were significantly lower 4.4 (2.0-9.0), 2.8 (1.7-4.7), 2.0 (0.9-4.8) respectively (Kruskal-Wallis p<0.0001). Similarly, u-NGAL was found at higher levels in A-LN patients, 3.3 (2.0-5.7) µg/mmol, with respect to the ANR-SLE 2.0 (0.9-4.5), I-SLE 1.6 (0.8-3.2), and HC 2.4 (1.2-5.3), (p=0.008). The highest levels of OPN were found in the group of I-SLE (190.6 (85.1-299.9) µg/mmol, compared to A-LN 72.98 (37.6-118.1), ANR-SLE 92.3 (58.5-129.7) and HC 76.5 (58.2-120.3), (p<0.0001). KIM-1 levels differed among groups with higher levels in the A-LN group (188.9 (113.7-309.7) ng/mmol), in comparison to ANR-SLE 131.4 (92.2-186.1), I-SLE 123.8 (70.3-200.2), and HC 78.2 (68.8-115.1), (p<0.0001). GAL3 showed comparable levels across groups. When exploring the biomarkers across histologic subgroups of LN, u-GAL3BP could discriminate between proliferative and mesangial forms (17.7(9.6-32.5) vs 6.7(5.1-16.1) ng/mmol, p=0.027), while it did not discriminate against membranous LN. U-NGAL was higher in proliferative LN 3.7(2.4-5.8) µg/mmol with respect to membranous 2.4 (1.1-3.8) (p=0.01), while mesangial LN showed comparable levels. OPN, KIM-1 and GAL3 were comparable across groups. In the ten patients with available samples after induction therapy (mycophenolate mofetil (MMF) in 4, rituximab (RTX) in one, cyclophosphamide in 5 (one combined with MMF and one with RTX), u-GAL3BP showed a significant decrease of median levels from 218.8 to 41.5 ng/mmol (Wilcoxon p=0.03). u-GAL3BP associated with renal activity in class III/IV LN (R=0.42, p=0.004).

Conclusion: Among the tested markers, high uGal3BP adjusted for creatinine was found to be a promising marker of renal involvement in SLE patients and associated with renal activity in patients with proliferative forms (class III/IV) of LN. A decrease was further seen following therapy, suggesting that u GAL3-BP could be used to monitor renal activity.

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POS0185

IDENTIFICATION AND VALIDATION OF TWO NOVEL SERUM BIOMARKERS ASSOCIATED WITH THE SEROLOGICAL STATUS OF RHEUMATOID ARTHRITIS PATIENTS.

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Background: Despite the diagnostic value of Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibodies (ACPA), more serological markers are needed in order to improve early diagnosis and treatment response of the Rheumatoid Arthritis (RA) patients. Increased knowledge about how these two major autoactivities arise is crucial for understanding how RA develops and what mechanisms drive pathogenesis.

Objectives: We aimed to investigate, using a proteomic strategy, novel protein biomarkers associated with RF and/or ACPA that might be useful to stratify seropositive and seronegative RA patients.

Methods: A shotgun proteomic analysis was performed on 80 sera from the RA cohort of the Rheumatology Unit of the University Hospital of Santiago de Compostela (CHUS). Sera were classified as seropositive or seronegative according to their RF and ACPA values, and were then analyzed employing the iTRAQ labeling technique (Sciex) followed by LC-MALDI-MS/MS analysis (MALDI-TOF). A Multiple Reaction Monitoring (MRM) method was subsequently developed using the Skyline Software for the simultaneous quantification of 26 peptides belonging to ten putative protein biomarkers. The quantitative targeted analysis was performed using peptides with isotope labelled amino acids as internal standards. Serum levels of orosomucoid 1 (ORM1) and haptoglobin (HPT) were measured using commercially available ELISA Kits in the whole RA cohort (n=260) from the Rheumatology Unit of the University Hospital of A Coruña (HUAC).

Results: For the initial screening, eighty sera were grouped according to the ACPA/RF status in 4 pools (20 patients/pool). Using an iTRAQ technology-based quantitative proteomic approach, the abundance of eleven proteins was altered in the sera from ACPA^{pos}/RF^{pos}, 13 proteins in ACPA^{neg}/RF^{pos} and 12 proteins in ACPA^{pos}/RF^{neg}, compared to ACPA^{neg}/RF^{neg}. Vitamin D binding protein (VTDB) was the unique protein that resulted increased in all the comparisons. For the biomarker verification phase, all the samples from the CHUS cohort were analyzed individually (n=80). Using the MRM technology, 26 peptides belonging to ten putative protein biomarkers associated with double positivity were simultaneously quantified. The statistical analysis showed a significant modulation of 9 peptides (belonging to 4 different proteins) in ACPA^{pos}/RF^{pos}, 7 peptides (5 proteins) in ACPA^{neg}/RF^{pos}, and 9 peptides (6 proteins) in ACPA^{pos}/RF^{neg} compared to ACPA^{neg}/RF^{neg} (p<0.05). Two acute phase reactants (ORM1 and HPT) displayed the same modulation in both screening and verification phases, thus confirming their association with the double positivity. Finally, in the biomarker validation phase, a total of 260 patients from CHUAC were included (Table 1). RA patients were classified as follows: (1) 112 patients (43.1%) were ACPA^{pos}/RF^{pos}; (2) 73 patients (28.1%) were ACPA^{neg}/RF^{neg}; (3) 51 patients (19.6%) were ACPA^{neg}/RF^{pos}; and (4) 24 patients (9.2%) were ACPA^{pos}/RF^{neg}. Serum levels of ORM1 and HPT (Figure 1), measured by commercial immunoassays, confirmed their increased values in double seropositive patients (p=0,0053 ORM1; p=0,0026 HPT). Finally, the increased level of ORM1 resulted associated with RF rather than ACPA status (p=0,0008 ACPA^{neg}/RF^{pos}); whereas HPT was associated with ACPA rather than RF status (p=0,0112 ACPA^{pos}/RF^{neg}).

Table 1. The different phases of RA biomarker development followed in this study.

	DISCOVERY	VERIFICATION	VALIDATION
	PHASE	PHASE	PHASE
Source center	CHUS	CHUS	CHUAC
Nº of samples	n= 4 ACPA+RF+ Pool 1 ACPA-RF- Pool 2 ACPA-RF+ Pool 3 ACPA+RF- Pool 4	n= 80 ACPA+RF+ 20 ACPA-RF- 20 ACPA-RF+ 20 ACPA+RF- 20	n= 260 ACPA+RF+ 112 ACPA-RF- 73 ACPA-RF+ 51 ACPA+RF- 24
Nº of biomarkers	ORM1, ORM2, HPT, A2GL, AACT, RBP4, PLMN, IC1, VDBP, APOB	ORM1, HPT, A2GL, AACT	ORM1, HPT

Figure 1: ORM1 levels are increased in RA patients seropositive for RF (499±437 µg/mL in ACPA^{neg}/RF^{pos} vs 300±248 µg/mL in ACPA^{neg}/RF^{neg}). HPT levels are statistically significant increased in RA patients seropositive for ACPA (3193±2233 µg/mL in ACPA^{pos}/RF^{neg} vs 2046±1795 µg/mL in ACPA^{neg}/RF^{neg}).

Figure 1.